

# EXHIBIT 13

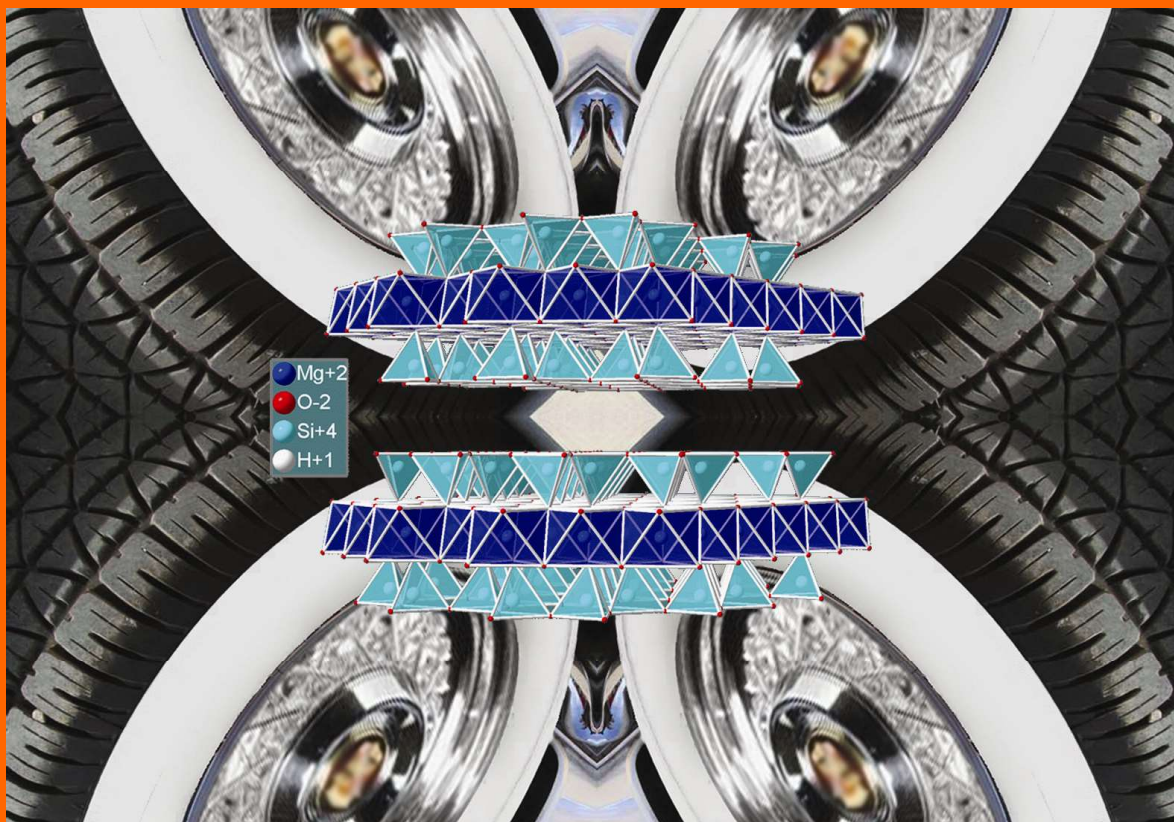
WORLD HEALTH ORGANIZATION  
INTERNATIONAL AGENCY FOR RESEARCH ON CANCER



# ***IARC Monographs on the Evaluation of Carcinogenic Risks to Humans***

## **VOLUME 93**

### **Carbon Black, Titanium Dioxide, and Talc**



LYON, FRANCE  
2010

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This publication represents the views and expert opinions  
of an IARC Working Group on the  
Evaluation of Carcinogenic Risks to Humans,  
which met in Lyon,

7–14 February 2006

2010

## IARC MONOGRAPHS

In 1969, the International Agency for Research on Cancer (IARC) initiated a programme on the evaluation of the carcinogenic risk of chemicals to humans involving the production of critically evaluated monographs on individual chemicals. The programme was subsequently expanded to include evaluations of carcinogenic risks associated with exposures to complex mixtures, lifestyle factors and biological and physical agents, as well as those in specific occupations. The objective of the programme is to elaborate and publish in the form of monographs critical reviews of data on carcinogenicity for agents to which humans are known to be exposed and on specific exposure situations; to evaluate these data in terms of human risk with the help of international working groups of experts in chemical carcinogenesis and related fields; and to indicate where additional research efforts are needed. The lists of IARC evaluations are regularly updated and are available on the Internet at <http://monographs.iarc.fr/>.

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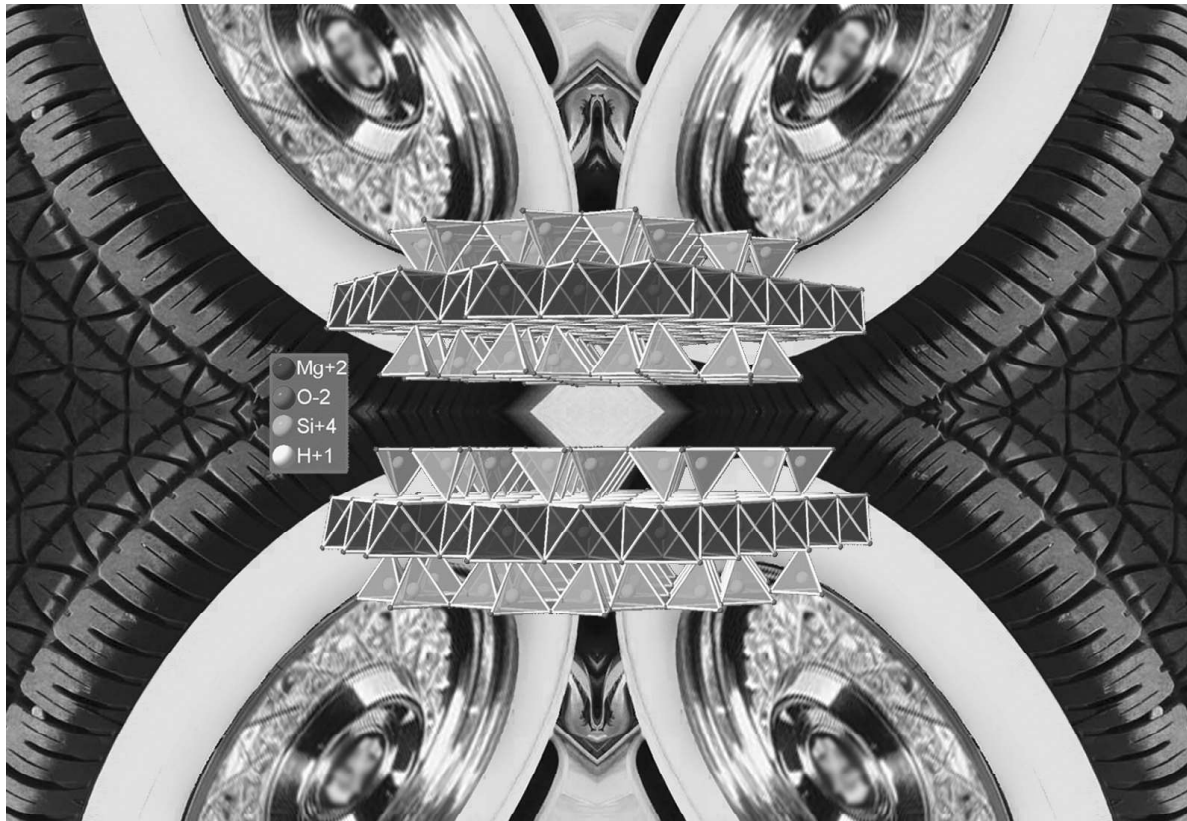
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Cover photograph: The white-wall automobile tyre represents carbon black and titanium dioxide; the chemical structure illustrates the platy structure of talc (see Section 1 for details).

Cover photograph and design: Roland Dray, IARC

Source of the talc structure: <http://en.wikipedia.org/wiki/File:Talc.GIF>

## GENERAL REMARKS

This ninety-third volume of *IARC Monographs* contains evaluations of the carcinogenic hazard to humans of three chemically inert, poorly soluble particles: carbon black, titanium dioxide, and talc. In 2003 an Advisory Group on priorities for future evaluation recommended that carbon black and titanium dioxide be considered with high priority (IARC 2003), and in 2004 an Advisory Group to plan a series of *IARC Monographs* on air pollution recommended that these particles be reviewed before complex mixtures such as diesel engine exhaust. Talc is included in this volume because as an inhaled particle it has many features in common with carbon black and titanium dioxide, and as a consumer product it has been the subject of an abundance of epidemiological studies. Each of the three agents in this volume has been reviewed before. Carbon black was evaluated in Volume 65, titanium dioxide in Volume 47, and talc not containing asbestiform fibres in Supplement 7. New epidemiological and experimental studies are reviewed in this volume.

This volume does not review carbon-based particles of more complex or variable composition, such as activated charcoal, toner, charbone, and soot. This volume also does not review ultrafine and engineered nano-forms of these particles, because there are few pertinent studies. The physical properties and mechanistic studies of ultrafine and nanoparticles that are reviewed in this volume suggest that these smaller particles, due to their greater surface area per unit of mass, may be more effective in inducing toxic effects.

The review of talc in Supplement 7 led to evaluations for two agents: talc containing asbestiform fibres and talc not containing asbestiform fibres. The term ‘asbestiform fibre’ has been mistaken as a synonym for ‘asbestos fibre’ when it should be understood to mean any mineral, including talc, when it grows in an asbestiform habit. To avoid confusion over the term ‘asbestiform fibre’, the present Working Group decided that it is scientifically more precise to call the agent ‘talc not containing asbestos or asbestiform fibres’, and this evaluation supersedes the earlier review of talc not containing asbestiform fibres. The present Working Group also decided to expand the name of the Group-1 agent from ‘talc containing asbestiform fibres’ to ‘talc containing asbestos or other asbestiform fibres’. The present Working Group reviewed the earlier *Monograph* on talc containing asbestiform fibres and determined that the expanded name is consistent with what had been evaluated in Supplement 7. No update was undertaken for this Group-1 agent.

## **TALC NOT CONTAINING ASBESTIFORM FIBRES**

### **1. Exposure Data**

#### **Introduction**

Talc refers to both mineral talc and industrial mineral products that are marketed under the name talc and contain proportions of mineral talc that range from about 35% to almost 100%.

The mineralogy of airborne particles in talc mines is restricted by that of the deposit and associated rocks. Therefore, mines and mills provide an opportunity to characterize exposure to one specific source of talc mineralogically. In contrast, the mineralogy of talc in an industrial setting where talc products are used may be difficult to characterize, because many different sources of talc are available for almost every application. Industrial talcs are quite variable in their talc content and in the identity and proportion of other minerals that they contain. In addition, talc is part of a complex mixture of materials in user industries.

Talc particles are normally plate-like. When viewed under the microscope in bulk samples or on air filters, they may appear to be fibres and have been identified as such. Talc may also form as true mineral fibres that are asbestiform; asbestiform describes the pattern of growth of a mineral that is referred to as a 'habit'. Asbestiform talc fibres are very long and thin and occur in parallel bundles that are easily separated from each other by hand pressure.

Asbestos is a commercial term that describes six minerals that occur in the asbestiform habit: actinolite, anthophyllite, chrysotile, grunerite, riebeckite and tremolite (IARC, 1977). Similarly to talc, these six minerals occur more commonly in a non-asbestiform habit, and may also be elongated without being asbestiform. Actinolite, anthophyllite and tremolite may occur in some talc deposits; when asbestiform, they constitute asbestos and, when not asbestiform, they are referred to as mineral fragments or cleavage fragments.

## TALC

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Table 2.1. Cohort studies of mortality from and incidence of cancer in populations occupationally exposed to non-asbestiform talc

Reference, location	Cohort description	Exposure assessment	Organ site	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors; comments
Rubino <i>et al.</i> (1976), Germanesca and Chisone valleys (Piedmont), Italy	1992 male talc workers (1514 miners, 478 millers) employed >1 year in talc-exposed job during 1921–1974; hired 1921–1950; mortality follow-up, 1921–74; vital status, 90%; cause of death: 95% of exposed workers, 95% of controls	Occupational history from plant records; respirable dust measurements, 1948–1974; quantitative estimation of cumulative exposure for individual workers, expressed as summed product of duration (years) and exposure (million particles per cubic foot, mppcf); classification of workers into 3 levels of exposure	All cancers	All miners	100	<b>SMR</b> 0.8 (0.6–0.9)	Adjusted for age; comparison with unexposed, age-matched controls from neighbouring rural town; controls matched on vital status at date of entry into study; miners and millers exposed to a very pure form of talc; miners also exposed to inhalable silica; significantly elevated SMRs for silicosis with and without tuberculosis among miners; estimates increased with increasing cumulative exposure; no observed cases of mesothelioma; no smoking data for exposed workers or unexposed controls
				All millers	42	0.9 (0.7–1.2)	
				<i>Miners (mppcf-years)</i>			
				Level 1: 566–1699	38	1.2 (0.8–1.6)	
				Level 2: 1700–5665	28	1.0 (0.7–1.4)	
				Level 3: 5666–12750	34	0.9 (0.6–1.2)	
				<i>Millers (mppcf-years)</i>			
				Level 1: 25–141	18	1.1 (0.2–3.2)	
				Level 2: 142–424	13	1.3 (0–2.9)	
				Level 3: 425–906	11	0.7 (0.4–2.7)	
			Lung, bronchus and trachea	All miners	9	0.5 (0.2–0.9)	
				All millers	4	0.6 (0.2–1.6)	
				<i>Miners (mppcf-years)</i>			
				Level 1: 566–1699	3	1.1 (0.6–1.7)	
				Level 2: 1700–5665	1	0.5 (0.7–2.3)	
				Level 3: 5666–12750	5	1.1 (0.4–1.3)	
				<i>Millers (mppcf-years)</i>			
				Level 1: 25–141	3	1.7 (0.3–4.9)	
				Level 2: 142–424	1	1.25 (0–7.0)	
				Level 3: 425–906	0	—	

Table 2.1 (contd)

Reference, location	Cohort description	Exposure assessment	Organ site	Exposure categories	No. of cases/deaths	Relative risk (95% CI)	Adjustment factors; comments
Rubino <i>et al.</i> (1979), Germanesca and Chisone valleys (Piedmont), Italy	1678 male talc workers (1260 miners, 418 millers); mortality follow-up, 1946–74	Same exposure categories as Rubino <i>et al.</i> (1976)	Lung	All miners All millers <i>Miners (mppcf-years)</i> Level 1: 566–1699 Level 2: 1700–5665 Level 3: 5666–12750 <i>Millers (mppcf-years)</i> Level 1: 25–141 Level 2: 142–424 Level 3: 425–906	8 4  2 1 5  3 1 0	<b>SMR</b> 0.5 (0.2–0.9) 0.7 (0.2–1.7)  0.5 (0–1.9) 0.2 (0.5–1.2) 0.6 (0.2–1.4)  2.0 (0.4–5.8) 0.7 (1.7–3.7) —	Re-analysis of cohort reported in Rubino <i>et al.</i> (1976); SMRs recalculated using national death rates instead of comparison with neighbouring rural population; national death rates available only from 1951 onward; rates for 1951 were applied for 1946–50
Selevan <i>et al.</i> (1979), Vermont, USA	392 white male talc workers (163 miners, 225 millers) employed >1 year between 1940 and 1969; mortality follow-up: date of first radiogram, 12-month employment anniversary or January 1940, whichever was later; follow-up through 1975; vital status: 99%; cause of death: 94%	Historical insufficient information to calculate cumulative exposure histories; cohort classified into two work areas: mining and milling.	All causes  All cancers  Respiratory cancer	Total cohort Millers Miners  Total cohort Millers Miners  Total cohort Millers Miners	90 44 34  16 5 7  6 2 5	<b>SMR</b> 1.2 [0.9–1.4] 1.2 [0.9–1.6] 1.3 [0.9–1.8]  [1.3 (0.7–2.0)] [0.8 (0.3–1.9)] [1.7 (0.7–3.5)]  [1.6 (0.6–3.5)] [1.0 (0.1–3.7)] [4.3 (1.4–10.1)]	Adjusted for age, sex, race, calendar year; US death rates: 1940–67; linear extrapolation for all causes of death: 1967–69. Vermont death rates for specific causes of death: 1949–75; workers selected from annual radiographic survey of dusty trades; no data on smoking habits for millers or miners; exposure to radon daughters in mine; radiographic evidence of pneumoconiosis in most workers who died from non-malignant respiratory disease